HCG when the leading follicle reached a diameter of 18-22 mm. He found that both doses, 3 and 1 mg per day, were sufficient for LH suppression without any differences.

This regime does not in any way anticipate either a long protocol for IVF with **only 0.25 mg** Cetrorelix starting on cycle day 6 up to ovulation induction with HCG nor a **single or dual dose** of preferably **3 mg** and the prevention of negative effects of HCG during luteal phase. The present application clearly discloses and claims a **multiple dosage regime** with preferably **0.25 mg** Cetrorelix **per day** or a **single or dual dose of preferably 3 mg**.

The skilled artisan would not have expected that such low doses of the LHRH antagonist Cetrorelix would have a sufficient effect. These treatment protocols were in no way anticipated by Diedrich and also improved the infertility treatment in a surprising and unpredictable manner. In addition, the economical benefit of low doses and low dosing frequency, respectively, is an additional advantage, since the antagonist is costly.

The present inventors have also enabled with their invention that FSH can be kept at physiological levels with only a dosage of 0.25 mg/day given on day 6-10. Therefore, it is not correct to say, as in the Examiner asserted in the Action of March 3, 1999, that Diedrich used the same methods and dosages as described in the present invention. The dosage of the present invention is only one quarter, related to 1 mg, and less than one tenth, related to 3 mg, of that used in the long protocol.

Claims 15, 16, 18-24 and 26-33 stand rejected under 35 USC § 103(a) as

being unpatentable over Diedrich et al. in view of Felberbaum et al. This rejection is again traversed for the following reasons.

Applicants note several points that distinguish the study in the Felberbaum et al. article from the claimed invention. Cetrorelix was introduced in the study IVF program to examine whether it is possible to avoid premature LH surge and to lower the interference with the hypothalamo-hypophysial-ovarian axis. The study design describes two different dose regimes with 3 mg Cetrorelix s.c. daily and 1 mg Cetrorelix daily from day 7 until ovulation induction. Premature LH sure could be avoided in both dosages. Nothing is reported about FSH remaining at a physiological level. This regime is therefore only in partial conformance with the invention. The work to elaborate a clinical practicable therapeutic regime is the contribution of Diedrich together with the other inventors of the present application who are not named as authors.

The advantage of the present invention lies in the development of a single or dual dose posology including preferably 3 mg Cetrorelix on cycle day 6 and a multiple dose posology representing a dose of 0.25 mg Cetrorelix beginning on cycle day 6. **Applicants respectfully submit that this is a remarkable difference in dose and management of IVF therapy resulting in surprising and unforseeable benefits for the patients.** In addition, neither of the cited references mentions the use of much lower dosage and thus do not provide any suggestion toward the more effective treatment process which results from the application of the present invention.

The Examiner found the Declaration filed November 23, 1998 to be unpersuasive, and stated that paragraphs 3 and 4 of the declaration appear to contradict each other. Applicants respectfully disagree.

The present application describes and claims the use of Cetrorelix in the IVF program to avoid premature LH surges, including application of FSH and LH for follicular stimulation followed by Cetrorelix application starting on day 6 and continuing up to ovulation induction with HCG, which is the subject matter of claim 15 and hence the same inventive entity.

The other inventors, who are not authors, contributed to the elaboration of a clinically practicable therapeutic regime, which is represented by a short or long-protocol treatment in which only 0.25 mg Cetrorelix is given until ovulation induction or a short protocol in which 3 mg is given once or twice up to ovulation induction. Thus, the Felderbaum article only describes a portion of the invention, as it does not include the particular regimes that are presently claimed.

In summary, in paragraph 3, it is stated that Diedrich and the other named inventors made the invention by a collaborative intellectual effort that resulted in the design of the clinical study. In paragraph 5 it is stated that the inventors, except for Diedrich, were not involved in carrying out the study in the sense that they did not physically participate in the work. It is submitted that these statements are not contradictory. Furthermore, the Examiner is reminded that authorship of an article by itself does not raise a presumption of inventorship with respect to the subject matter disclosed in the article. In re Katz, 215 USPQ 14 (CCPA 1982).

Claims 15, 16, 18-24 and 26-33 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending application 09/053,152. This rejection is noted and Applicants will consider filing a Terminal Disclaimer if the '152 application is allowed prior to the present application.

Claims 21 and 22 have been provisionally rejected as claiming the same invention as that claimed in claims 34 and 35 of "prior U.S. Pat. No. 09/053,152". Should overlapping claims in the '152 application be allowed, Applicants will consider cancellation of such claims in the present application.

All objections and rejections having been addressed, it is submitted that the application is in condition for allowance, and Notice to that effect is respectfully requested.

Respectfully submitted,

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